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Disease-a-Month

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Biliary Tract Disease

ALBERT I. MENDELOFF
CHARLES ECKERT

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Biliary Tract Disease

ALBERT I. MENDELOFF
CHARLES ECKERT

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DISORDERS of the gallbladder and the extrahepatic biliary tree represent commonly occurring causes of abdominal complaints. The detection of the underlying pathophysiology, the exercise of judgment in trying to decide whether the patient's symptoms really result from the demonstrated lesion, and the approach to proper therapy represent one of the most fascinating intellectual disciplines the physician is called on to exercise. In few other areas of the body can physician and surgeon complement each other so satisfactorily. Advances in antibacterial therapy and in surgical technic, combined with better preoperative care, have reduced sharply the mortality of surgical intervention for the relief of these diseases, and postoperative management has correspondingly been made somewhat simpler. It is the purpose of this treatise to deal in moderate detail with some of the more controversial aspects of therapy of these disorders, against a background of the anatomic and physiologic derangements which com-

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prise the major symptomatic entities. The discussion will not deal in a direct way with disorders of the liver or of the pancreas.

NORMAL ANATOMY AND PHYSIOLOGY OF THE BILIARY TRACT

Anatomic Features

Formed originally from the ventral diverticulum of the foregut, the extrahepatic biliary tree branches out from the hepatic diverticulum to form the hepatic and common ducts, the cystic duct, and its terminal pouch, the gallbladder. This arborizing system is embryologically first a solid core, then goes through a hollowing-out process. The peculiarities of the growth of the ventral diverticulum and interruptions in the process of canalization probably account for the many variations in anatomic features encountered by the surgeon in his dealings with the right upper quadrant of the abdomen.

The intrahepatic portion of the biliary tree is formed as a single duct in the left lobe of the liver, and as two ducts in the larger right lobe. All three of these usually merge at the quadrate lobe, either just at or just outside the hilum, to form the common hepatic duct, a structure 3.0 to 3.5 cm. in length. This short tube receives from the right anterolateral direction the coiled cystic duct; below this junction the duct is called the common bile duct, measuring 9 to 12 cm. in length and 5 to 7 mm. in diameter, with a wall approximately 0.5 to 1.0 mm. in thickness. The common duct in about one third of subjects is in its terminal portion entirely extrapancreatic, in another third entirely intrapancreatic, and in another third the terminal portion is partly within and partly without the pancreas. The terminal portion of the duct is termed the ampulla, but actually the external dilatation of this portion conceals the fact that internally the duct narrows to a very thin nozzle-like lumen, which is separated from a similarly narrow channel arising from the pancreatic duct by a thick mass of muscle and connective tissue. This entire area encounters the duodenal serosa at an angle of 45 to 80°, traverses the muscular coat of the duodenal wall in a gentle curve, then thrusts itself into the lumen almost perpendicularly to the long axis of the duodenum.

Elaborate dissections of this area seem to show that the common bile duct and the pancreatic duct form a "common

channel" proximal to the papilla of Vater in about 32% of all subjects; the two ducts empty separately in about 40%, and in another 28% the "common channel" is distal to the sphincteric muscle, but is very short (less than one third the length of the papilla) (1). The nipple of the papilla is usually about 2 mm. in diameter, and projects above the duodenal epithelium in about 60% of subjects, being either level with or below the epithelium in the other 40%.

The gallbladder is a thin-walled bulbous sac capable of holding 80–100 ml. of fluid when fully distended, but in its resting stage containing 30 ml. of bile. It occupies a concavity on the inferior surface of the liver, and empties into the cystic duct, which proceeds cephalad and posteriorly to join the common hepatic duct. The neck of the gallbladder is guarded by the special "valves" of mucosa forming the first portion of the cystic duct, which averages about 3 cm. in length.

The entire extrahepatic biliary tree, developing as it does from a single anlage, receives its innervation from both splanchic and vagal fibers, and stimulation of various portions of this tree is poorly localized by the brain. Even after complete bilateral vagotomy and celiac ganglionectomy it has been shown that some components of the phrenic nerve reach the biliary tract through hepatic veins and peritoneal reflections.

Control of Flow in the Biliary Tree

Hepatic bile is probably formed continuously under a low secretory pressure (less than 350 mm. of bile). Pressure in the gallbladder in its resting stage is always less than 100 mm.; thus, if the sphincter of Oddi is closed hepatic bile enters the gallbladder. The sphincter resistance in man normally varies from 75 to 250 mm. Uncompensated elevations of sphincter resistance to levels above 600 mm. of bile will stop hepatic excretion of bile, and if maintained will cause dilatation of the gallbladder and biliary tree.

In the fasting state very little bile enters the duodenum. With the ingestion of food the sphincteric muscles relax, and bile gushes into the duodenum in nonrhythmic squirts. The duration of bile flow depends on the amount of bile in the gallbladder and the pressure relationships in the ducts between the liver and the duodenum. The cystic duct offers little resistance to flow in either direction, and bile ordinarily enters the gallbladder at all times except when it is fully dis-

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tended or actively contracting. The stimulus for gallbladder contraction is the hormone cholecystokinin, which is produced by duodenal mucosa on contact with acidic chyme and fats. The stimulus or stimuli controlling the four intrinsic muscles of the sphincter of Oddi have not been clarified, but it is clear that the action of these muscles is to erect the papilla and to close it. Whether the sphincter responds primarily to pressure changes in the duodenum or in the biliary tree, to nervous impulses, or to chemical contact is not certain. Animal studies show that removal of a normal gallbladder causes the sphincter to become incompetent, allowing bile to dribble into the duodenum in an irregular fashion. Vagal impulses can increase sphincteric resistance, and spinal anesthesia can reduce it. Sphincter resistance decreases somewhat after ingestion of a fatty meal, and also on contact with magnesium ions. Various drugs increase sphincteric resistance—morphine and codeine most strikingly, methadon and demerol® much less so—and nitrates, nitroglycerin, and atropine (large doses only) decrease it.

Diagnostic Methods Applied to the Biliary Tract

1. *Cholecystography*

   (a) Historically, the demonstration by Graham and Cole in 1924 that intravenously injected tetraiodophenolphthalein caused the gallbladder to be visualized by x-ray was one of the major advances in diagnostic medicine. Since that time many refinements have been made in the technic of this examination, and newer materials readily absorbed from the gut have proved satisfactory as contrast media. All of them depend on (1) adequate absorption from the small bowel, (2) excretion by the liver into the biliary tree, and (3) sufficiently concentrated media in the ducts and gallbladder to produce a photographic image. Recent materials have elicited much less nausea and vomiting than was the case with older media, so that problems in technic today revolve principally around failure of a diseased liver to handle the dye arriving via the blood stream, and insufficient radiopacity due to the dye being poorly concentrated by a diseased gallbladder, or excessively diluted by diffusion throughout an enlarged collecting system.

   The examination should always begin with a plain

film of the right upper quadrant, using a Bucky diaphragm and intensifying screen. The patient must hold his breath, and the exposure time be made as short as possible. The positioning of the patient is of the utmost importance; the prone position is most satisfactory, and an inflated balloon under the epigastrium helps limit movement. If this film shows any opacification in the right upper quadrant, tomography is probably indicated to define the shadows further.

The details of the procedure for oral cholecystography vary in different clinics, but usually, after an enema or castor oil the afternoon before the day of examination, the patient takes the prescribed number of capsules of the dye (the dose is on the basis of body weight), then eats a light fat-free supper. Nothing further is ingested until the patient reports in the morning for the examination. At this time films are made of the right upper quadrant in the prone and upright positions, using anteroposterior, left anterior oblique, and lateral projections. A right lateral decubitus position with tube directed horizontally may demonstrate layering of stones, the cholesterol stones tending to float.

A fat-rich meal is then administered, and the films repeated one or two hours later. The contraction of the gallbladder elicited by this meal may serve to localize stones not clearly seen when the organ is full of dye, or to concentrate shadows very faintly seen prior to the meal, but has no other diagnostic importance.

If no visualization of the gallbladder is reported to the referring physician, what is his next step? First, he should carefully question the patient as to whether the ingestion of the dye was followed by nausea, vomiting, or diarrhea. If the physician strongly suspects the presence of biliary tract disease, and the patient had no trouble with the dye ingestion, the oral cholecystogram should be repeated. If on two occasions properly performed tests fail to visualize the gallbladder, and marked hepatic disease is absent, gallbladder disease may be presumed to be present.

(b) What place has intravenous cholangiographic tech-

nic in the demonstration of gallbladder disease? In the series of cases so far reported, a number of patients without previous gallbladder surgery, but with non-visualization of the gallbladder after oral cholecystography, have been subjected to the procedure, using cholografin® as the contrast medium. One third of these patients have shown x-ray visualization of the gallbladder, including demonstration of calculi. Some of these at operation have had obstruction of the cystic duct. Thus it may be tentatively assumed that visualization of the biliary ducts without visualization of the gallbladder is proof presumptive of gallbladder disease. Since the cholografin® technic demands intravenous injection and meticulous control of many details by the radiologist, it should be reserved for those cases in which nonvisualization of the gallbladder after oral cholecystography does not satisfy the physician that gallbladder disease is present.

On the other hand, intravenous cholangiography is the procedure of choice when the gallbladder has been surgically removed, when biliary dyskinesia is suspected, or when symptoms suggestive of fistula formation or of common duct obstruction are present. The dye is usually employed as a 20% solution, the total dosage being 30–50 ml. The rapidity with which this material is cleared by the liver, and the necessity for relying on films every 15 minutes for two hours to note the degree of filling of the ductal system, demands the complete personal attention of the radiologist for this period of time. In addition, reactions to the intravenous injection of cholografin®, although rarely serious, are often distressing and require constant watchfulness. The rate of reactions is approximately 15%, most of these being nausea, vomiting, pruritus, urticaria, and mild circulatory abnormalities—extrasystoles, palpitation, dizziness. In some clinics 20 mg. of diphenhydramine are given intravenously prior to injection of the dye; the dye solution is injected in the amount of 1 ml., and, if no reaction has occurred within 5 minutes, the remainder of the dose is given. Patients with impressive allergic histories may either be refused the dye, or given intensive antihistaminic

or cortisone therapy for several days prior to the injection.

The transfer of cholografin® from blood to bile demands more nearly normal liver function than does the transfer of oral cholecystographic media. It has been repeatedly shown that patients carrying a serum bilirubin level greater than 5 mg. per cent cannot concentrate cholografin® sufficiently in the biliary tree to justify the use of the test.

In summary, then, the intravenous cholangiogram is of primary importance in attempting to delineate (1) the morphology of the extrahepatic biliary tree in the cholecystectomized patient and (2) the presence of an obstructive lesion, stricture, or calculus in the common duct when jaundice is minimal. In order for the radiologist to realize its potentialities, the test should be combined with tomography for sharp photographic definition of the common duct. Standards for diameter, length, and configuration of the common duct in the cholecystectomized patient are at present still being derived, and the importance of time-density curves in evaluating the freedom of bile flow in the common duct has been stressed. It appears that normal common ducts show loss of radiopacity 45–60 minutes after injection of cholografin®; persistence or increase of radiopacity after 60 minutes correlates well with obstruction to bile flow in the common duct.

But the physician also may have a different problem. The radiologist may report that the oral cholecystogram is normal, despite the symptoms suggestive of biliary disease. In this case the physician may request that the test be repeated, but that the dose of dye be cut in half. This may serve to demonstrate small calculi obscured by the intense concentration of opaque media in the usual test. If the use of the reduced dose still does not demonstrate gallbladder disease, the physician must turn to duodenal aspiration to confirm his clinical diagnosis.

(c) The time-honored technic of directly intubating the second duodenum for withdrawal of secretions still has a place in the diagnosis of biliary tract disease. In fact, the new interest in exfoliative cytology has re-emphasized the importance of looking carefully at

biliary tract sediment. The principle of the test consists largely in the separation of aspirate into three portions: The "A" fraction—the mixed secretion lying in the lumen of the duodenum; the "B" fraction—that derived from drainage of the lower common duct after sphincteric resistance has been lowered by instillation per tube of magnesium sulfate, and consisting principally of gallbladder bile; finally the "C" fraction thought to come from the hepatic ducts. The sediment must be centrifuged at 3000 rpm. in order to bring crystals down in so surface-active a fluid. The presence of cholesterol crystals and calcium bilirubinate sludge in the sediment of either "A" or "B" fractions has as high a correlation with the presence of cholelithiasis as does "non-visualization" of the gallbladder by cholecystography. Exfoliated cells may be studied by the Papanicolaou technic applied to the same sediment. Duodenal aspiration after intravenous injections of secretin or decholin® in the normal subject shows a prompt drop in the icteric index of the aspirate—i.e., the choleretic effect of the injected drug is associated with an increase in sphincter resistance, so that the increased biliary output is driven into the gallbladder. If the gallbladder is diseased or has been removed, the duodenal aspirate continues to show the presence of bile after injection. Of course, in the presence of complete obstruction of the common duct, no bile is obtained in any specimen.

Disorders of Function in the Biliary Tree

Aside from the manifestations of acute and chronic inflammation of the gallbladder, which will be discussed separately, most of the symptoms experienced by human patients with disease in this area of the body are due to derangements in motor activity. As is usually the case in an enclosed fluid system emptying into a larger, unenclosed system, the principal difficulties ensue when the final valve controlling flow loses its ability to compensate rapidly and smoothly for pressure changes in front of or behind it. Although this seems obvious enough, analysis of the pathophysiology of the biliary tract is made extraordinarily difficult because of our

lack of understanding of the factors governing normal pressure-flow relationships.

1. *Biliary Colic*

Although one may oversimplify by speaking of "typical" symptoms of biliary tract diseases, biliary colic itself displays fairly constant features. The patient has an abrupt onset of epigastric or right upper quadrant pain, varying in degree from mild to extraordinarily severe; associated with the pain, which in our experience is rarely intermittent, is difficulty in drawing a deep breath, and a characteristic restlessness; the patient cannot lie in bed, tries to find comfortable positions without avail, and usually walks about for several hours before relief occurs spontaneously or after the physician has administered an analgesic. Nausea and vomiting may accompany both common duct obstruction and cystic duct blockage. Experimental distention of the gallbladder does not produce nausea and vomiting in man, but the deep-seated abdominal discomfort resulting closely resembles that seen in severe biliary colic. If the cystic duct or common duct is distended, nausea and vomiting occur. Pain referred to the epigastrium suggests that a peritoneal reaction has occurred. Pain referred to the interscapular area or to the right scapular or supraclavicular area is presumed to occur as a result of local irritation of branches of the phrenic nerve, which have been demonstrated to enter the hepatobiliary system via hepatic veins, but critical analysis of studies so far reported makes one hesitate to accept this explanation unreservedly. Certainly pain referred to the shoulder tip is unusual. The attacks tend to come on during the night after especially heavy meals, and when they recur in the same person follow a monotonous pattern, differing principally in severity and duration. Frequently the patient complains of "soreness" in the subcostal area for a period of 12–36 hours after the attack begins.

2. *Biliary Dyskinesia*

The physiologic literature on resistance to pressure in the ductal system is complicated by the use of different laboratory animals, artificial experimental conditions, and observations on human patients suffering from diseases of this system. That these relationships are altered in human patients who have undergone cholecystectomy seems certain, and may explain syndromes of spasmodic right upper quadrant and epigastric pain resembling that of established biliary tract disease, but only rarely associated with jaundice.

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It is the contention of many surgeons that long-standing symptoms of this type are associated with anatomic changes in the papilla, principally hypertrophy and fibrosis, with narrowing of the lumen. They postulate that this anatomic change results from a persistent disturbance of function, a failure of relaxation, requiring higher pressures to be built up behind the papilla, further irritating the latter. Symptoms of this type seem to develop more frequently in patients whose gallbladder prior to excision had functioned reasonably well. One may speculate that in such patients when the biliary tree suddenly assumes the volume-compensating action previously carried out by the gallbladder, dysfunction of the papilla results. Other conditions may affect the action of the sphincter in normal animals; thus reflex changes in bile flow have been demonstrated in dogs by distention of the colon, the bile output being reduced in volume and increased in viscosity. Similarly, stimulation of the colonic or inferior mesenteric plexus in the dog increases sphincteric resistance significantly. These reflex effects may explain the clinical correlations between colonic dysfunction and symptoms referable to the biliary system. They suggest that conservative management of patients suffering from such symptoms, particularly after cholecystectomy, should always precede more drastic and perhaps dangerous attempts to disrupt the musculature of the sphincter. The use of intravenous cholografin® to demonstrate the caliber of the common duct is of particular assistance in this type of patient.

GALLSTONES

Concretions in the gallbladder have long been recognized as a concomitant of aging, the prevalence in autopsied populations showing a high correlation with increasing age. In the United States the prevalence of gallstones of all types is variously reported to range from less than 1% in the first two decades of life to 40% in females over 70 years of age, and to 25% in males of the eighth decade. At age 50 a conservative estimate would be that 15% of women and 5 to 8% of white men have cholelithiasis. The disease is distinctly uncommon in the negro male, but the negress differs less significantly from the white female in susceptibility to the disease. The marked sex difference in prevalence has always seemed to implicate pregnancy as a factor in the genesis of gallstones, but the increasing frequency with

which stones are found after women reach the age of 50 would require at least an alternate explanation.

It is probably logical to consider that gallstones are formed whenever physicochemical changes in the bile favor precipitation of the substances found on chemical analysis to comprise the concretions. It is obvious that such changes may result from abnormalities originating in the bile secreted by the liver and hepatic ducts before arrival in the gallbladder (i.e., hepatogenous factors), or from disturbed function of the gallbladder in handling the material once it arrives (vesical factors). In most instances the causes are multiple, and changes in the gallbladder wall may be the result of the presence of stones as well as a cause contributing to their formation. Whether or not sluggish emptying of the gallbladder—so-called biliary stasis—is an entity independent of the above is not clear; statements made stressing the importance of such an abnormality are based on occasional x-ray abnormalities seen in pregnant women, for example, or on equations between sedentary habits and "poor gallbladder tone." Most of the attempts to implicate a stasis factor have been made in order to replace the older theory incriminating bacterial infection as the primary cause of gallbladder disease, a concept which originally was strengthened by the prevalence of typhoid fever and its frequent involvement of the gallbladder. Since that disease has become a rarity, but gallstone formation seems to proceed as usual even in the antibiotic era, infection with pathogenic bacteria must play a very minor role in initiating the processes which lead to cholelithiasis.

Chemical analysis of the gallstones formed in diseased human gallbladders has been performed for decades, and much speculation has arisen therefrom as to the pathogenesis of this serious and common affliction. Except for calcium bilirubinate stones all concretions encountered in the gallbladder have a somewhat similar composition, being formed of cholesterol, or of cholesterol plus calcium carbonate around a nucleus of softer amorphous debris; most chemical studies of the bile have been directed to analyzing the physicochemical factors governing the solution of cholesterol in this fluid. Bile acids, cholesterol, free fatty acids, and the phospholipid lecithin are the most important constituents. Methodologic difficulties in the past have prevented general agreement among investigators as to the chemical fractionation of bile from normal and pathologic

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gallbladders, but in the past few years newer technics have been applied to these problems, with more clear-cut results. According to Isaakson (2), the total bile salts account for 50 to 60% of the total solids of bile; when lyophilized bile is subjected to fractional chloroform extraction, all the lecithin and most of the bile salts appear in the chloroform extract; this lecithin-bile salt mixture has a great ability to keep cholesterol in aqueous solution. Of the total bile salts of bile, 65 to 75% participate in the lecithin-bile salt system (hereafter called LBS). Fractionation of the three major bile salts show that cholic acid participates in this system to a greater extent than do chenodesoxycholic or dehydrocholic acids.

The cholesterol content of normal human gallbladder bile is very high, about 600 mg. per 100 ml. Since cholesterol is very slightly soluble in water, its constant solubilization in bile must require an active participation by the LBS system; bile salts alone cannot dissolve more than a small fraction of biliary cholesterol. Isaakson found that one equivalent of cholesterol required the presence of ten to twelve equivalents of the LBS system for total solubilization; there was no difference in this requirement in bile obtained from pathologic gallbladders, but the total cholesterol of such bile reached two to five times the concentration in normal bile, and 72 to 93% of all pathologic bile samples examined had a lecithin-bile salt: cholesterol ratio of less than 11:1, the critical ratio for keeping cholesterol in solution.

These observations cannot be interpreted more precisely, since the disturbed ratio can be accounted for on the one hand by increased cholesterol production or decreased cholesterol absorption, or, on the other hand, by decreased production or increased absorption of the lecithin-bile salt components. In addition, the total solids in pathologic bile are considerably reduced, but it is possible that this merely reflects a diminished absorptive power of the gallbladder mucosa for water. In general terms, gallstones formation is favored:

1. Whenever the gallbladder wall has undergone an inflammation ,which impairs its ability to absorb water, increases its absorption of bile salts, or causes epithelial cells to be desquamated.

2. Whenever abnormal hemolytic mechanisms fill the gallbladder with bile more heavily laden with bilirubin than normal.

3. Whenever general or local conditions in the body put more cholesterol, or less phospholipid, or both, into the hepatic bile entering the gallbladder.

It is generally agreed that the plasma cholesterol increases during pregnancy; according to Boyd (3) the phospholipids and fatty acids of serum rise concomitantly, so that the serum phospholipid-cholesterol ratio is not altered. The rise in serum cholesterol begins in the third month and rises to a peak at the thirtieth week of pregnancy, at which point it diminishes, so that in Boyd's study there was little or no elevation of free cholesterol, esterified cholesterol, or phospholipid concentrations in the serum at the eighth month of pregnancy as compared to postpartum levels. The rise in total serum cholesterol may reach values twice the normal level, although concentrations 25 to 50% higher are much more commonly encountered. There is some difference of opinion as to whether the rise is accounted for principally by free cholesterol, which seems better documented, or by parallel increases in the free and esterified fractions. There is no evidence that the increase results from impaired hepatic excretion of cholesterol. Serum lipids are reported by Boyd to fall rapidly as soon as women lactate, all fractions being within the normal range as soon as lactation is well established. Neutral fat concentration, although much more variable, tends to be definitely elevated in the serum of pregnant women, and to fall rather more slowly after delivery than do other lipid fractions.

The reasons for these lipid changes are obscure. Isaakson was able to raise or lower the concentrations in bile of both cholesterol and of the LBS system by raising or lowering the fat content of diets fed to calves; the critical ratio between the two fractions remained undisturbed. With regard to the way gallstones actually form, colloid chemistry theory leads to sharp disagreement with the older concept of the slowly enlarging gallstone, growing by layering of calcium carbonate and cholesterol around a core of desquamated epithelium. Such studies as those of Weiser and Gray (4) would lead one to believe that gallstones form as masses of cholesterol, protein, and lime salts in the colloidal state, within which the Liesegang phenomenon occurs at some later date, resulting in the loss of water and emergence of a crystalloid state, which characterizes the gallstone as seen at operation or autopsy. The production of gallstones in the Syrian hamster by Dam and Christensen (5), who fed them a fat-free

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diet, has been confirmed by Fortner. (6) In these animals the gallbladder contained a thick mucinous material in which the stones were embedded; the appearance of the stones would favor the hypothesis that a change from a colloid to a crystalloid state had occurred. The absence of fat from the diet of these animals conceivably leads to gallbladder atonicity, and presumably stasis of its contents under these circumstances would occur. Some reported stones are so large as to suggest the conversion of the entire vesical contents into a single crystalloid. The role of free fatty acids in gallstone formation remains a subject of dispute.

The entity known as cholesterosis consists of submucosal lipid and cholesterol deposits throughout the gallbladder. The lipoid deposits are found in the phagocytes of the submucosa, and at the base of the mucosal cells. Usually the individual deposits are rather small, but very large deposits may cause papillomatous enlargement of the villi, producing the x-ray picture of a polyp. The apparent propensity for these deposits early to be concentrated near the cystic duct, plus the rather uniform disturbance in the secretory glands of this region, suggest that a mechanical or inflammatory dysfunction of the vesical neck may be responsible for the condition. The concomitant presence of gallstones in cases with cholesterosis (50 to 80% of reported surgical cases) can be interpreted to show that the condition is a manifestation of the same difficulty in cholesterol solubilization as that which accounts for stone formation. On the other hand, some autopsy figures reveal this disease to be more common in males; cholecystograms in those cases not associated with stones are often normal, the percentage reported varying from 40 to 80%; some autopsy figures reveal coexistence of cholesterosis and gallstones in as few as 2.5% of subjects. Significant association of cholesterosis with various forms of liver disease and with acute and chronic pancreatitis has been reported. Unless stones are present, the disease apparently produces no symptoms and has no significant relationship to carcinoma of the gallbladder.

The composition of gallstones is such that at least 15% are visible in the plain x-ray films of the right upper abdomen; these usually show a thin rim of calcium around a non-opaque core. Laminations are occasionally seen, and multiple stones are usually faceted. Bilirubin stones are very small and tend to be round; it is of interest that they contain enough calcium bilirubinate to be radiopaque in nearly the

FIG. 1.—Solitary radiopaque stone visualized on plain x-ray examination. Note the laminations.
FIG. 2.—Solitary radiolucent stone.

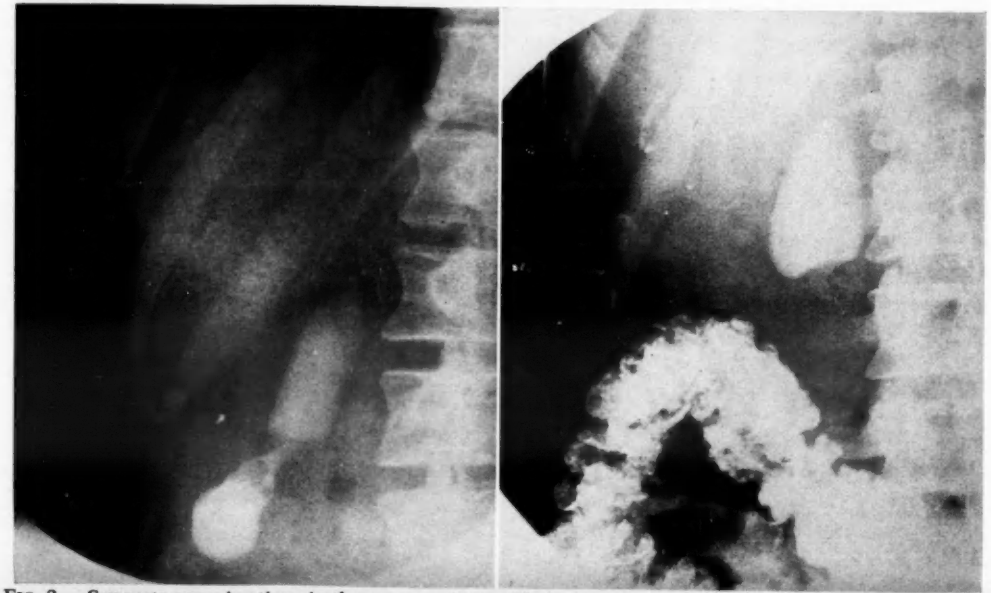

FIG. 3.—Separate examinations in the same patient with 2 years intervening. The central hourglass contracture became complete. Operation for acute cholecystitis.

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FIG. 3.—Separate examinations in the same patient with 2 years intervening. The central hourglass contracture became complete. Operation for acute cholecystitis.

FIG. 4.—Multiple radiolucent stones.
FIG. 5.—Calcification of the wall of the gallbladder. Chronic cholecystitis.

same proportion as the more common mixed stones, but this may be due to the fact that the gallbladders in chronic hemolytic diseases are literally packed with these calculi.

THE MECHANISM OF OBSTRUCTIVE JAUNDICE

For many years investigators have tied off the common bile duct of experimental animals and observed the histologic changes induced in the liver and biliary tract. Early studies showed that within 24 hours after such ligation in the rat the centrilobular areas of the liver showed accumulation of bile pigment and isolated parenchymal cell necrosis. In man the study of early obstructive jaundice by needle biopsy of the liver has demonstrated that rather marked changes can be identified within the first week of jaundice; according to Sherlock (7), these comprise centrilobular bile pigment deposition, cellular necrosis in the midzonal and periportal areas, and bile duct proliferation in the portal areas. Bile pigment accumulates in the parenchymal cell cytoplasm and as isolated "bile thrombi" in the canaliculi.

Exactly how these changes come about is still disputed. Recent studies by Hanzon (8) in the rat, which has no gallbladder, seem to show by a fluorescein technic that 8 to 15 minutes after common duct ligation the bile canaliculi begin to dilate, and eventually to rupture. In the periphery of lobules lakes of dye were noted after 48 hours, representing either leakage from larger ducts, or massive necrosis of many cells with common collecting ductules. The leaking bile itself seems to be toxic to hepatic cells, so that obstruction in the biliary tree damages the liver cell both by a mechanical rupture of canalicular membranes and by a toxic injury from the high concentration of bile bathing the cell after canalicular rupture. Bile production depends on adequate hepatic blood flow, favorable pressure gradients, and cellular integrity; anoxia and hypothermia markedly reduce the capacity of parenchymal cells to secrete bile.

Once obstruction to bile flow occurs in man, whether as the result of constriction of the terminal portion of the common duct, of narrowing of the extrahepatic biliary tree at any point, or of obliteration of sufficient numbers of the tiniest collecting ducts in the interlobular areas of the hepatic parenchyma itself, a series of symptoms and signs follows. The symptom of obstruction which is of particular significance is pruritus, usually mild at the onset, but relentlessly

intensified as the obstructive process continues. Anorexia, epigastric fullness, and abdominal pain are much more variable when obstruction is due to extrahepatic causes, and it is remarkable how poor a correlation there may be between the extent of the obstructive process and the severity of symptoms. The rate of enlargement of the liver in obstructive jaundice is conditioned by the presence or absence of a functioning gallbladder. The lack of the gallbladder, whether by surgical removal, cystic duct obstruction, or fibrotic scarring, greatly decreases the capacity of the biliary ductal system, so that the rate of bilirubin accumulation in the serum and of hepatic enlargement may be very rapid, at first. After some days this process slows down, however, and further enlargement of the liver, in the experience of the authors, depends on the development of cholangitis, tumor metastases, or biliary cirrhosis.

Fever is a common accompaniment of calculous obstruction of the biliary tract, often being the only sign produced in elderly patients with no icterus, slight pruritus, and a common duct literally packed with stones. True shaking chills usually indicate the presence of cholangitis, and are unusual in other forms of jaundice. The stools vary in color as obstruction is incomplete or complete, from pale tan to cement-gray; the presence of significant amounts of occult blood in repeated stool examinations suggests the presence of a malignancy of the pancreas or papilla, but an occasional stool positive for blood may be associated with calculous obstruction. Complete obstruction to bile flow for any length of time may lead to the development of symptoms secondary to the absence of bile from the intestine; the most important of these is purpura on the basis of hypoprothrombinemia; less common is the inception or exacerbation of a duodenal ulcer, or the development of a malabsorption syndrome.

On physical examination a distended gallbladder almost always signifies that a malignancy is obstructing the common duct. Epigastric masses arising from the pancreas may be diagnostic. The syndrome of vascular spiders, enlarged spleen, and xanthelasmata provides evidence for a diagnosis of biliary cirrhosis of advanced degree.

It is probably true that 85% of all patients presenting with jaundice can be correctly diagnosed by the history, physical examination, and routine laboratory study of blood, urine, and stool. Special laboratory tests are reserved for the 15% who present more difficult diagnostic problems; of

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those, the most vexing is certainly the patient who has intrahepatic obstructive jaundice—i.e., a perfectly normal extrahepatic biliary system, but a rather selective lesion involving the cholangioles, behind which bile regurgitates and fails to reach the duodenum. In such cases, in the absence of a clear-cut history of preceding hepatitis, or of receiving methyl

TABLE 1.—LABORATORY DATA HELPFUL IN THE DIFFERENTIAL DIAGNOSIS OF JAUNDICE

	HEPATOCELLULAR JAUNDICE	CHOLANGIOLITIC JAUNDICE	EXTRAHEPATIC OBSTRUCTIVE JAUNDICE
WBC	Usually normal, with relative lymphocytosis	Usually normal, with normal differential	Usually elevated, with shift to left
Urine urobilinogen concentration	Rarely absent for $>$ 7 days; often very high	Low values for weeks	Low to absent early; absent later
Fecal urobilinogen	Usually normal or low	Very low	Low to absent
Turbidity and flocculation tests	Strongly positive	Usually negative	Negative unless cholangitis has occurred
Serum transaminase	High	Normal	Normal or slightly elevated
Alkaline phosphatase of serum	Usually $<$ 12 B.U.	Usually $>$ 12 B.U.	Almost always $>$ 12 B.U.
Response of lowered prothrombin concentration to parenteral vitamin K	Minimal	Returns to normal	Early—complete return to normal Late—partial return to normal

testosterone, arsenicals, or chlorpromazine, it is next to impossible to state with certainty that the patient does not have a lesion for which surgery is indicated. Although it may provide little assistance, a needle biopsy may on occasion be the only way to make this differential diagnosis, and this type of case constitutes an important indication for the use of this procedure.

When jaundice is due to extrahepatic obstruction, the bi-

opsy needle may transfix a dilated bile duct of moderate size, an accident which almost always results in bile peritonitis. It is recommended that in such patients neither needle biopsy nor peritoneoscopic biopsy be performed, but rather that the patient have surgical biopsy under direct vision.

Because liver function tests are often relied on to differentiate jaundice due to hepatitis or cirrhosis from that consequent on an extrahepatic obstruction, we have listed the tests which in our hands are of the most value for this purpose. (Table 1) It is suggested that whole batteries of tests not be repeated at regular intervals, since no two tests require the same number of days in which to attain maximally significant values. The icteric index is as useful as the van den Bergh in following the intensity of jaundice; the urine urobilinogen concentrations, observation of the color of the stools, and the differential white blood cell count are inexpensive and highly informative when performed daily or every other day. In the patient wth a serum bilirubin level greater than 5 mg. %, tests which rely on the integrity of the parenchymal cells plus biliary pathways in the liver should *not* be carried out; such tests would include the bromsulfalein retention, oral cholecystogram, or intravenous cholografin® procedures. Flat films of the right upper quadrant and duodenal drainage may, however, be of particular value in such cases.

DISEASES OF THE GALLBLADDER

Congenital Anomalies

Congenital anomalies involving the gallbladder are rare, particularly if one excludes those associated with atresia of the bile ducts. A knowledge of the different anomalies which have been described is of great importance to the surgeon who may encounter them in the course of operations on the biliary tract. These include absence of gallbladder, reduplication in whole or in part, and anomalies of position. Ten cases of absence of the gallbladder were collected from the records of the Mayo Clinic by Dixon and Lichtman (9). That the gallbladder is absent on rare occasions must be remembered in interpreting non-visualization of the gallbladder in cholecystography.

A variety of forms of reduplication of the gallbladder are described. Bifid gallbladder with a common cystic duct, com-

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plete reduplication of the vesicle with separate ducts, the two vesicles lying in close relation to each other, or entirely separate gallbladders are among the forms of this anomaly which are seen. At times there is an anomalous point of entry of the cystic duct or ducts into the hepatic ducts.

Included in the anomalies of position are those cases in which the gallbladder is entirely within the liver, left-sided gallbladder, and free-floating gallbladder. When an intrahepatic gallbladder is the seat of empyema, the difficulties of surgical treatment are magnified. The free-floating gallbladder is completely enveloped in peritoneum, the mesentery is short, containing the blood supply, lymphatics, and nerves. This anomaly is of particular clinical significance because it is prone to undergo torsion or volvulus. The twist is in a clockwise direction varying from 90–360 degrees. Gross (10) described 50 cases of torsion; 42 were in females, 8 in males; the average age was 59, but the greatest incidence was noted in the eighth decade of life. The symptoms which are seen consist of intense right upper quadrant pain, nausea, and vomiting. On physical examination tenderness and muscular rigidity in the right upper quadrant are found. The gallbladder is palpable in some cases. It is apparent that unrelieved torsion will result in the rapid development of gangrene; this therefore represents a true surgical emergency inasmuch as walling off is prevented by the rapidity of the process.

Cholecystitis

The mechanical disturbances which result from the presence of stones in the gallbladder and bile ducts are of basic importance in the development of the inflammatory diseases of these structures. Until gallstone formation can be prevented, or until stones can be dissolved in vivo by a specific chemotherapeutic agent, these diseases will continue to present a challenge to the medical profession. There is no evidence of a decreasing incidence of biliary tract disease today; in fact it is likely that unless specific measures to influence stone formation become available, these diseases are destined to increase in frequency along with the increasing life expectancy of the population. Because of the importance of mechanical factors in the production of symptoms it is not surprising that surgical removal of stones is necessary in order to prevent the continuation of symptoms or to prevent the development of complications. Unfortunately, the simple

removal of stones is only temporarily effective; since the factors conducive to stone formation are unaltered, stones tend to re-form with greater or lesser rapidity. Although removal of the gallbladder will prevent the further formation of stones in most cases, it is not justifiable to remove the gallbladder prophylactically or in the absence of definite intrinsic disease. The penalties paid by the patient for injudicious or technically inferior surgery in this area are great. Persistent disability from unrelieved symptoms, or chronic invalidism from strictures of the common bile duct, are two of these sequelae. On the other hand, the proper selection of patients and skillful operation will combine to yield excellent results.

Studies of the age distribution of patients reveals that cholecystitis increases constantly with age for each decade of life in proportion to the number at risk in each decade. However, no age group is exempt from the development of cholecystitis. It is extremely rare in the first decade of life, only two cases being recorded at the St. Louis Children's Hospital. Griffin and Smith (11) found 6.2% of the patients to be below the age of 25. Women are affected more commonly than men; the proportion in a group of 650 patients reviewed from the files of the Barnes Hospital was 3 to 1. In this group of patients 95% had stones. Chronic cholecystitis is seen with greater frequency than acute cholecystitis. In the series referred to above 16% had the acute form of the disease. Holden (12) reported the incidence of acute cholecystitis to be 20% in his series.

Etiology. Our knowledge of the etiology of cholecystitis is incomplete. It is likely that different factors are responsible in varying proportions for the initiation of the inflammatory process. The concept that cholecystitis is the result of primary bacterial infection dates back to Virchow's studies of typhoid cholecystitis. This concept was generally accepted until Drennan (13) cast doubt on its validity by culturing the bile from 100 gallbladders involved in cholecystitis. Feinblatt (14) noted that the pathologic appearance was not suggestive of bacterial inflammation. The particularly thorough studies of Andrews and Henry (15) are responsible for the general acceptance of the secondary role played by bacterial infection. In 68 cases of cholecystitis careful cultures were obtained from bile and the gallbladder wall; the bile was found to be sterile in 65% of cases, the wall in 51%. Growth in the positive cultures was almost always

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scanty with the exception of those cases in which E. coli was cultured. Aronsohn and Andrews (16) were unable to produce cholecystitis in dogs when the gallbladder was inoculated by atraumatic technic with large numbers of different pathogenic bacteria. They pointed out that previous investigators who had reported the production of cholecystitis in animals through the inoculation of the gallbladder had always injured the gallbladder by the process of injecting their cultures. In the same report Aronsohn and Andrews showed that bile salts or normal bile concentrated to 50% of its initial volume, when injected by the same atraumatic technic which failed to produce cholecystitis with bacteria, now produced changes characteristic of cholecystitis seen in humans. Desoxycholanic acid was a more potent irritant than glycocholic acid. Womack and Bricker (17) confirmed these observations. Cole (18) was able to produce similar changes in the wall of the gallbladder in dogs by partially obstructing the neck of the vesicle. In some of these animals stone formation was also observed. Ligation of the cystic artery and control operations without obstruction failed to produce the same changes. Wolfer (19) demonstrated that pancreatic juice might reflux into the gallbladder and that it was capable of producing cholecystitis. Bisgard (20) also carried out experiments to demonstrate the importance of pancreatic juice in the genesis of cholecystitis.

Observations in the operating room indicate that complete obstruction of the cystic duct through the impaction of a stone is an important factor in clinical cholecystitis. In addition to the factor of concentrated bile which is trapped in the gallbladder, interference with venous and lymphatic flow results; this undoubtedly contributes to the development of acute inflammation and may be responsible for focal necrosis. Obstruction of the cystic duct, if unrelieved, results in either hydrops or empyema. In the former, the normal constituents of the bile disappear and are replaced by a clear viscid mucoid fluid which distends the vesicle. The wall is thin and shows little evidence of cellular infiltrate. In empyema, the wall of the gallbladder thickens, largely due to edema, but cellular infiltration is also prominent. The bile is replaced by a grossly purulent fluid. Examination of this fluid in some cases reveals that it is truly pus, in other cases polymorphonuclear leukocytes are scanty, calcium carbonate and cholesterol crystals are abundant. When pus is present secondary bacterial invasion is likely. The explanation for

the response of hydrops or the appearance of empyema without gross infection is not clear.

Occasionally cholecystitis is a manifestation of a systemic disease; polyarteritis nodosa can cause gangrenous cholecystitis following cystic artery thrombosis.

ACUTE CHOLECYSTITIS. Patients previously free of complaints referable to the biliary tract may develop acute cholecystitis; in 95 to 98%, however, the patient will have had either previous acute inflammation or symptoms of chronic cholecystitis. In either case the disease is characterized by acute pain in the right upper quadrant or epigastrium, radiating to the tip of the scapula or back, associated with nausea, vomiting, and fever. On physical examination tenderness and muscle spasm in the right upper quadrant are found. The gallbladder or an inflammatory mass is palpable in some cases. The intensity of the pain is variable; in severe attacks it has periods of crescendo intensity alternating with other periods during which it is less severe although still present. Fever is usually of low grade; when high it should occasion suspicion of perforation. Leukocytosis of 10,000 to 15,000 is usually seen. Elevation of the total white blood cell count in excess of 20,000 should give rise to the suspicion that complications have occurred. In most cases the attack will begin to subside in 72 to 96 hours. Patients are also seen with acute biliary colic in whom the symptoms subside following a single injection of morphine. Rapidly progressive forms of acute cholecystitis are encountered; torsion of the free-floating gallblader is one example, serious impedance of venous return with focal areas of necrosis due to impaction of a stone another. In our experience free perforation of the gallbladder is rare, but walled-off perforation in the form of pericholecystic abscess is somewhat more common. Cowley and Harkins (21) found 23 cases of perforation of the gallbladder in a series of 490 cases operated on for acute cholecystitis, an incidence of 4.7%. Free perforation was present in 6, or 1.2%. Only one of these patients with free perforation died. The remaining cases had walled-off perforations or perforation into an adjacent viscus. In a review of 2261 cases from the literature they found the incidence of perforation to be 13%. Holden (12) found 9 perforations in 315 acutely inflamed gallbladders, an incidence of 2.8%. Three of these were free perforations, with one death.

Jaundice occurring during the course of acute cholecys-

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titis is seen in approximately 20% of cases. The severity is variable. Mild icterus without obstruction to the flow of bile occurs. In these cases the possibility of pericholangitis is likely. The failure to demonstrate stones on common duct exploration does not exclude the possibility of small stones which have been spontaneously passed. When obstructive jaundice is seen with acute cholecystitis, fever, prostration, persistent vomiting, and extracellular fluid deficits are all likely to be severe.

Differential Diagnosis. Acute appendicitis, perforated duodenal ulcer, acute pancreatitis, renal lesions, right lower lobe pneumonia, and acute myocardial infarction are most troublesome in differential diagnosis. Holden (12) emphasizes the discrepancy between the clinical and the pathologic diagnosis of acute cholecystitis, when disease in the gallbladder is responsible for symptoms. A careful history and physical examination, x-rays of the abdomen and chest, and the electrocardiogram will all aid in establishing the correct diagnosis. Cholecystograms and duodenal drainage are of little value during the acute episode. An interrelationship between acute pancreatitis and biliary tract disease is known to exist in certain cases. The serum amylase determination, frequently considered to be specific for acute pancreatitis, will not exclude the diagnosis of acute cholecystitis. Bernard and Criscione (22) reviewed a series of 52 cases from the Barnes and St. Louis City hospitals in which the serum amylase was elevated. In 36 the amylase was over 1000 Somogyi units, in 7 it was 500 to 1000 S.U., and in 9 it was under 500 S.U. In 14 of 28 patients who were operated on, examination of the pancreas was negative or equivocal, but all had disease in the gallbladder and common bile duct. In only 3 patients was significant involvement of the biliary tract not discovered.

Treatment. The variations in the natural history of acute cholecystitis are at least partially responsible for the arguments which have arisen over conservative *vs* surgical treatment of acute cholecystitis. The comparison of statistics collected by individuals favoring each side does not give conclusive answers to the question of which is the preferable form of therapy. If the case reports of patients who have died as a result of acute cholecystitis are perused it is impossible to tell whether the outcome would have been different had the other form of therapy been used. The over-all mortality rates for either method of treatment are quite

good; in general the risk is greatly increased in patients over 50. Since in all series the group of patients with previous attacks is far in excess of those who are seen in the initial attack the conclusion is inevitable that cholecystectomy earlier in the course of their disease would eliminate many of the seriously ill patients from this group.

The arguments which have been advanced by the more vocal advocates of either extreme therapeutic viewpoint are summarized in Table 2. There can be little disagreement

TABLE 2.—Arguments Used by Proponents of Conservative vs. Radical Treatment

Acute Cholecystitis	
Conservative	Radical
Perforation infrequent	Perforation frequent
Operative risk increased	Operative risk no greater in first 72 hours
Two operations may be required	When necessary, cholecystostomy is life-saving
Risk of erroneous diagnoses great	Erroneous diagnoses can be minimized
Common duct exploration frequently omitted	Explorations done when indicated
	Period of hospitalization and disability is shortened

with the thesis that cholecystectomy early in the course of acute cholecystitis can reduce the period of disability. Edema, which is the most striking pathologic feature of early acute cholecystitis, is an aid rather than a hindrance to the technical removal of the gallbladder. Increased vascularity, vascular adhesions to omentum and contiguous viscera, and pericholecystic abscess all tend to increase the difficulty of cholecystectomy. These changes increase with the passage of time; within 48 to 72 hours of the onset of symptoms they are minimal. The region of the common bile duct can be dissected only with difficulty if these changes are present in this area. When dense adhesions, increased vascularity and abscess are present the surgeon may elect to perform cholecystostomy rather than risk injury to the structures in the porta hepatis by undertaking cholecystectomy. Elective cholecystostomy in the aged, debilitated patient with associated

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cardiovascular disease can be life-saving. However, cholecystostomy in a patient whose disease can be controlled by conservative measures adds an additional operative procedure. The niceties of judgment which are involved in the decision for performing cholecystostomy or cholecystectomy result from experience; the "occasional" surgeon in this area is likely to make the wrong decision to the detriment of the patient. In Table 3 the frequency with which cholecystostomy

TABLE 3.—CHOLECYSTOSTOMY FOR ACUTE CHOLECYSTITIS

AUTHOR	TOTAL OPERATIONS	CHOLECYSTOSTOMY	%
Glen (23)	697	61	8.75
Mustard and Custer (24)	36	8	22
Wallace and Allen (25)	415	138(?)	33
Zollinger and Cutler (26)	156	28	17.9
Dunphy and Ross (27)	134	20	15
Buxton, Ray, and Coller (28)	73	31	42.4

was deemed necessary relative to cholecystectomy in different institutions is given. The variation is between 8.75 and 30%. Wallace and Allen (25) in discussing the 30% incidence of cholecystostomy in their series compared the duration of disease, delay in operation, presence or absence of gangrene in the wall of the gallbladder in the two groups

TABLE 4.—COMMON DUCT EXPLORATIONS, ACUTE CHOLECYSTITIS

AUTHOR	TOTAL OPERATIONS	DUCT EXPLORED		STONES RECOVERED		
		No.	%	No. Cases	% of Explorations	% of Total
Holden *et al.* (12)	315	57	18	22	38.6	6.9
Glenn (23)	697	61	10	40	66	5.7
Dunphy and Ross (27)	134	56	41.8	28	50	20.7
Buxton, Ray, and Coller (28)	42	9	21.4	4	44.4	9.5
Zollinger and Cutler (26)	156	57	36.5	23	40.3	40.3

of patients and were unable to find a significant difference in any of these factors.

Inflammatory alterations in the region of the common bile duct may not only result in increasing the hazard of cholecystectomy but may obscure findings in the duct which would lead to exploration, or reduce the surgeon's inclination to explore the ducts. From Table 4, where data concerning the frequency of associated choledochotomy and the frequency of positive exploration are given, it is also to be noted that considerable variation exists. It is somewhat difficult to reconcile the difference between a 5.7 and 40.3% incidence of calculi in the choledochus by a variation in the selection of material. This point will be discussed in greater detail subsequently.

The operative mortality shown in Table 5 from a group of reports with divergent methods of treatment is obviously

TABLE 5.—MORTALITY, ACUTE CHOLECYSTITIS

AUTHOR	TREATMENT	NO. OF PATIENTS	NO. OF DEATHS	%
Holden *et al.* (12)	Early surgery	315	8	2.5
Glenn (23)	Early surgery	697	19	2.7
Zollinger and Cutler (26)	Early surgery	146	4	2.6
Doubilet *et al.* (29)	Nonoperative	116	1	0.84
Mustard and Custer (24)	Early surgery	36	2	5.5
	Nonoperative	172	3	1.7

very low. It is unlikely that it will be further reduced except by the performance of cholecystectomy at an earlier stage in the natural history of the disease.

Our own practice is to attempt to select patients for treatment according to the individual situation which exists. Younger good-risk patients who are seen within 72 hours in whom the diagnosis appears definite are operated on at the completion of study. This consists of plain x-ray films of the abdomen and chest in addition to the usual investigation. Time is also taken to administer intravenous fluids when significant dehydration is present. Because of the increased frequency of complications of acute cholecystitis in the diabetic patient, these individuals are likely to be treated by early operation. Because of delays before admis-

sion, and the time required to treat the diabetic state it is unusual in our experience to be able to operate in the early, optimum period. If during the time spent in treating diabetes prompt regression of symptoms does not occur, operative intervention is certainly indicated. The remaining, and larger proportion, of patients are treated conservatively under close observation in the hospital. Patients who are vomiting have a gastric tube passed for constant suction. Extracellular fluid and electrolyte deficits are corrected, demerol® being used to control pain. Anticholinergic drugs are indicated to reduce spasm of the sphincter of Oddi. Broad coverage antibiotics are used for the control of the secondary bacterial growth which occurs. In the event that signs of inflammation progress, symptoms are unimproved, or progressive leukocytosis ensues, operative intervention is indicated, regardless of the time which has elapsed since the onset of symptoms. The presence of jaundice is in our opinion an indication for conservatism, unless the jaundice is definitely subsiding. Acute cholecystitis in pregnancy is considered by some to be an absolute indication for early surgery, but we have not altered the foregoing general principles under this circumstance. Should indications for surgical intervention develop in patients with serious constitutional disease or in the aged, debilitated patient a planned cholecystostomy under local anesthesia can be life-saving.

CHRONIC CHOLECYSTITIS. In contrast to the symptoms produced by acute cholecystitis those resulting from chronic inflammation of the gallbladder are frequently vague and nonspecific. In some patients a history of previous acute cholecystitis is obtained. A distinctive history of biliary colic is very helpful in arriving at the correct diagnosis. Vague epigastric distress following meals, particularly the ingestion of fats, is not uncommon. Dyspeptic complaints, belching, bloating, flatulence, pyrosis, sour eructations may constitute the principal manifestations of the disease. The majority of patients with chronic cholecystitis have stones within the gallbladder either as cause or result of the inflammatory process. Jaundice occurs in 10% of patients sometime during the course of the disease. Since at age 50 gallstones, as previously mentioned, are seen in at least 15% of women and 5–8% of men, the coincidental occurrence of gallstones with nonspecific symptoms of this variety can be anticipated and a too-ready acceptance of this cause and effect relationship can result in error.

The physical examination in chronic cholecystitis is of value only when positive signs are present. Mild tenderness in the right upper quadrant is particularly likely during an episode of pain. Pain resulting from sharp percussion at the right costal margin (Murphy punch) is occasionally noted. In the presence of hydrops a large, bulbous, cystic mass is frequently palpable. Tenderness is often minimal. Jaundice resulting from the obstruction of the common duct by stone may be present.

The diagnosis of chronic cholecystitis is made on the basis of the history of biliary colic and the roentgenographic demonstration of gallstones. In many patients the gallbladder shadow will not be visualized on x-ray study. When this occurs repeat examination is indicated. It is important to control all aspects of the x-ray study, to be certain that the dye is ingested at the proper time, and that vomiting does not occur. If repeated examination results in persistent non-visualization the examination of the duodenal drainage may be of great assistance. The latter test is also of value when a normal gallbladder shadow is obtained in a patient with a suggestive history of chronic cholecystitis inasmuch as small stones may not be seen because of the density of the shadow produced by some of the newer dyes. These points have been discussed in Normal Anatomy and Physiology of the Biliary Tract.

Differential Diagnosis. The symptoms produced by gastroduodenal ulceration are at times confused with those arising in the biliary tract. Inasmuch as the incidence of cholecystitis is greater in patients who have chronic peptic ulcers, when roentgen evidence of cholelithiasis coexists with a duodenal deformity prolonged observation of the patient maintained on an adequate ulcer regimen will be necessary to determine the contribution of each lesion to the patient's illness. When the upper gastrointestinal tract is studied, attempts to demonstrate an esophageal hiatus hernia should be carried out. Esophageal hiatus hernias also are found in increased numbers in patients with biliary tract disease, particularly in older age groups.

In at least ⅓ of cases of pancreatitis, cholelithiasis and chronic cholecystitis will be observed. This relationship has been referred to previously in regard to elevated amylase levels in acute cholecystitis. When disease of the biliary tract occurs in association with pancreatitis, a clear-cut

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indication for cholecystectomy, choledochostomy, and possibly sphincterotomy exists.

The pain of angina pectoris is sometimes referred to the upper abdomen and may be confused with biliary colic. Patients above the age of 50 with gallstone disease have a greater than expected frequency of associated cardiovascular disease. Babcock (30) in 1909 called attention to this frequent association. FitzHugh and Wolferth (31) noted that flat or inverted T waves in the electrocardiogram prior to surgery might revert to normal, subsequent to adequate biliary tract surgery. Gilbert *et al.* (32) were able to demonstrate a decrease in coronary blood flow on distention of the gallbladder in the dog. Ravdin, Royster and Sanders (33) reported on the production of pain typical of angina pectoris by distention of the common bile duct following choledochostomy in patients with gallbladder disease and angina. Numerous clinical observations have also been made of the close relationship between gallstone disease and angina pectoris. It is now apparent that appropriate biliary tract surgery is strongly indicated in patients who have gallstones in conjunction with cardiac disease. A reduction in frequency and severity of cardiac symptoms can be anticipated, as well as actual prolongation of life. Surgery in this group of patients can be carried out without great increase in risk provided complications are avoided. The principal contraindication to surgery under these circumstances is the presence of a recent unstabilized myocardial infarct. Under this circumstance operation should be deferred from 3 to 6 months.

Renal calculi, neoplasms, diverticulitis of the colon, injuries to the dorsal spine, and other lesions have been confused at times with chronic cholecystitis. In the patient whose symptoms are not clearly defined it is important to consider these possible lesions before embarking on definitive treatment of biliary tract disease. Patients who have been inadequately studied and subjected to cholecystectomy are likely to increase the number of patients with persistent symptoms following operation.

Stones in the Common Bile Duct

Stones which are found in the extrahepatic bile ducts are usually formed within the gallbladder, reaching the ducts by passage through the cystic duct. It is true that

under some circumstances stones will actually form within the bile ducts; this is more likely following cholecystectomy than it is in the presence of a functioning gallbladder. In autopsy studies, stones in the bile ducts are found in over 20% of cases of cholelithiasis. The symptoms produced by stones in the bile ducts are the result of obstruction of the duct by the impaction of a stone, most commonly in the region of the ampulla of Vater, or the result of the passage of stones through the sphincter of Oddi. The clinical picture is classically characterized by obstructive jaundice, in association with biliary colic, nausea, vomiting, chills, and fever. Jaundice is, however, present only 53–76% of cases in different published reports. Jaundice, when present, is variable in intensity and is seldom complete. Chills and fever accompanying jaundice are indicative of ascending cholangitis. The pain produced by common duct stones is located in the epigastrium. It can be reduplicated by distention of the duct after choledochostomy. Pain is absent in 10% of the cases of obstructive jaundice due to stones. Frequent episodes of biliary colic are suggestive of the passage of stones into the common bile duct. Nausea and vomiting accompany attacks of pain. Zollinger (34) emphasizes the significance of marked spontaneous vomiting in the diagnosis of choledocholithiasis.

Treatment. There is no predictably satisfactory medical therapy for the patient with chronic cholecystitis and cholelithiasis. Medical therapy either tries to "rest" the gallbladder by dietary restriction or else tries to "exercise" the biliary tract by a daily morning regimen of magnesium sulfate to relax the sphincter of Oddi, followed by olive oil ingestion to cause the gallbladder to contract. This regimen also makes use of oral bile salts or bile acid preparations to promote choleresis. Both technics require antispasmodics, and often the use of nitrates to control acute attacks. Both therapeutic schemes may allay symptoms and convey the benefits attendant on careful regulation of daily living habits while the underlying disease continues its natural evolution. Our preference is for the former regimen when conservative treatment is indicated.

In the patient who has sought medical attention because of episodes of pain, when the diagnosis of gallstones is made, surgical removal of the gallbladder is indicated. In the patient with predominantly dyspeptic complaints suggesting dysfunction of multiple organ systems, it is much

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less likely that the removal of the gallbladder will result in striking improvement. The decision for or against surgery in such a patient is made on the basis of prolonged study and observation. The question also arises whether removal of the gallbladder is indicated when asymptomatic stones are discovered. There is evidence which indicates that comparatively few cases will remain free of symptoms if followed for a reasonable period of time. Since the complication rate and operative risk are increased with advancing age, in view of the exceedingly low operative risk of elective cholecystectomy in the asymptomatic individual it would seem reasonable to recommend cholecystectomy in selected patients with "silent stones." Practically, one usually watches the young patient with cholelithiasis for several years to determine the frequency of attacks, unless pancreatitis or marked evidence of debility occur.

The need for cholecystectomy for chronic non-calculous cholecystitis seldom arises in our experience. This diagnosis is made by the clinician more easily than it is confirmed by the critical pathologist. The fact that biliary colic occurs in patients with fibrous and round cell infiltration of the gallbladder in whom stones are not demonstrated does not exclude the previous passage of a small stone. Preston (35) has stressed the importance of benign obstruction at the sphincter of Oddi in the etiology of chronic non-calculous cholecystitis. Under these circumstances it is important to explore the common bile duct; failure to pass a probe into the duodenum is an indication for duodenotomy and retrograde investigation of the ampulla. Biopsy is advised if the papilla is prominent. For benign stricture, gentle dilatation or sphincterotomy should suffice to correct the defect.

The results of cholecystectomy in the treatment of chronic cholecystitis with stones are very satisfactory. The operative mortality in uncomplicated cases is under 1%. The operative morbidity is correspondingly low. Complete relief of symptoms is achieved in 90% of cases. The persistence of symptoms after cholecystectomy results from either errors in the selection of patients for operation, in technical errors on the part of the surgeon, or from dyskinesia. It is beyond the scope of this paper to consider in detail all the technical aspects of the biliary tract; however, the common errors responsible for poor results will be discussed.

The retention of stones in the common bile duct is probably the most frequent source of continued symptoms fol-

lowing cholecystectomy. The indications for the exploration of the common bile duct at the time of cholecystectomy are generally agreed on; it is therefore surprising to find wide divergence in not only the frequency with which exploration is carried out, but also in the frequency with which stones are removed. The indications which we believe should be followed are as follows:

1. History or presence of jaundice.
2. Palpable stone in the common bile duct.
3. Dilatation of the lumen of the common bile duct.
4. Thickening of the wall of the common bile duct.
5. Dilatation of the cystic duct.
6. Small stones in the gallbladder.
7. Evidence of pancreatitis.
8. Sediment in bile aspirated from the common bile duct.
9. Evidence of a stone on operative cholangiogram.

Not all surgeons agree with the usefulness of operative cholangiography. Like all diagnostic methods it is not devoid of false positives and negatives. These will be minimized as experience with the method increases. In view of the apparent imperfections in the surgical approach to common duct stones a technic as hopeful as operative cholangiography deserves full exploitation.

Waugh, Johnston and Cain (36) found that 27% of a group of 175 patients with common duct stones had had previous biliary tract surgery, either cholecystectomy alone or in combination with common duct exploration. Glenn (41), who has had similar experience, points out that patients with persistent symptoms are likely to change surgeons for their next operation. Therefore, unless direct follow-up information has been obtained, the surgeon cannot interpret the failure of patients to return with persistent symptoms as indicative of good results.

In Table 6 are given data from different surgical centers showing the comparative frequency and results of exploration of the common bile duct. The variations are striking. McKittrick and Wilson (39), reporting on 100 consecutive explorations carried out with cholecystectomy, found 52 with stones. This is considerably in excess of the number which would be anticipated. The size of the series and chance selection is probably responsible for the extreme frequency of choledocholithiasis in this series. By comparison, Glenn's figures indicate a lower than expected fre-

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quency of common duct stones. The follow-up of two separate groups from the New York Hospital series indicates that when exploration was not carried out 4% later had proved stones on reoperation. When stones were found on exploration 9% later had persistent stones removed, and when negative exploration had been carried out 4% had stones removed at later operation. Glenn points out that similar studies for comparison are not available. Certain it is

TABLE 6.—COMMON DUCT EXPLORATION COMBINED WITH CHOLECYSTECTOMY

AUTHOR	TOTAL OPERATIONS	DUCT EXPLORED		STONES RECOVERED		
		No.	%	No. Cases	% of Explorations	% of Total
Cattell (37)	1,104	504	45.7	186	36.7	16.8
Walters (38)	1,259	301	24	150	50	12
McKittrick and Wilson (39)	100	100	100	52	52	52
McLaughlin and Kleager (40)	230	71	30.7	—	33.8	10
Glenn (41)	2,472	259	10.5	179	69.1	7.2

that follow-up studies would reveal comparable evidence of persistent or missed stones.

The problem obviously involves not only the indications for exploration, but the actual procedure of exploring the bile ducts. Small stones in the hepatic ducts may be inaccessible. Stones impacted at the ampulla of Vater are also missed with greater frequency than stones in the remainder of the duct. Fragments of crushed stones when left in the ducts can serve as the nidus for formation of another calculus. Stones potentially will at times be passed into the gastrointestinal tract. It is likely that gentle, moderate dilatation of the sphincter of Oddi will facilitate the passage of small residual stones. Zollinger (42) has shown that forceful dilatation of the sphincter increases the perfusion and ductal pressures to twice the normal values. Thus the passage of stones may actually be impeded by this measure. Minimal dilatation did not influence the pressure recordings.

Another source of continued symptoms following cholecystectomy is the amputation of the gallbladder at the neck, or the division of the cystic duct at some distance from the point of junction with the common duct. In either of these circumstances stones may be left behind, or stones may possibly be formed within the stump of the gallbladder which was not removed. We have seen concentration of dye and x-ray visualization of the remaining gallbladder on several occasions. Womack and Crider (43) found neuromatous proliferation in the stump of the cystic duct to be responsible for persistent symptoms in 4 cases. During the past year we have seen a large neuroma involving the stump of the cystic duct in one patient with persistent symptoms.

When gallbladder disease coexists with pancreatitis, further symptoms may be prevented by cholecystectomy or the removal of a stone from the common duct. Doubilet and Mulholland (44) emphasize the role of sphincterotomy in patients with pancreatitis and gallstone disease. Failure to carry out sphincterotomy is responsible in some cases for persistent symptoms. However, the injudicious performance of sphincterotomy cannot be condoned. While Doubilet and Mulholland report excellent results with the use of this procedure, it has not gained widespread acceptance. In our opinion it should not be carried out unless obstructing fibrosis exists or unless chronic recurrent pancreatitis is present which has not responded to removal of the gallbladder, exploration and decompression of the common duct, and conservative measures. When sphincterotomy is performed it is our preference to do it under direct vision through a duodenotomy incision.

The management of the patient with obstructive jaundice of gallstone origin requires special mention. The usual patient with partial obstruction of recent origin in whom impaired liver function from cholangitis is minimal, is easily treated. Operation can be carried out at any time with small risk to this patient. When, however, jaundice has been present for several weeks, along with intermittent fever, nausea, and vomiting, proper preparation of the patient and selection of the time for operation are of great importance. Under these circumstances the administration of vitamin K to correct the bleeding tendency resulting from prothrombin deficiency is sometimes crucial. The level of circulating

prothrombin is estimated by the determination of the "prothrombin time." The procedure most commonly used for this purpose is that of Quick, although numerous modifications exist. Quick's method consists of the addition of an excess of calcium ions and thrombokinase to oxalated blood. Levels below 50% of normal are indicative of a coagulation defect; therefore correction is necessary before surgery is undertaken. Vitamin K administration will rapidly correct the prothrombin deficiency if the liver is functioning normally. The preparations in common use are the synthetic derivatives of 1, 4 naphthoquinone which is the basic ring in the naturally occurring vitamin K_1 and K_2. The addition of a methyl group at carbon 2 forms menadione which is water-insoluble and possessed of a high degree of K activity. Further modifications of the side chains form water-soluble compounds with similar activity. These materials can be administered orally, subcutaneously, intramuscularly, or intravenously. When water-insoluble preparations are given orally to the jaundiced patient bile salts must also be given to assure adequate absorption. It is our practice in preparing the jaundiced patient with hypoprothrombinemia for surgery to use 4 mg. of menadione or 10 mg. of one of the water-soluble modifications per day intravenously. The patient with obstructive jaundice without associated liver disease will usually have reached safe levels of prothrombin activity within 24 hours. The response however should be checked by repeated determinations of the prothrombin time in each patient.

The damaged liver can be protected against the further insult of the anesthetic agent by the administration of a high protein, high carbohydrate diet. In the patient who is able to tolerate oral intake, this is the preferable route of administration. In the patient who has anorexia, presentation of the diet in palatable form is frequently important. When the patient is vomiting, the replacement of extracellular fluid and electrolyte deficits, along with whole blood or serum albumin as needed, should be carried out. In our opinion operation is best deferred until jaundice is diminishing and the other measures can be accomplished. Constantly increasing icterus is more likely to result from neoplastic obstruction than from a gallstone. The more critically ill the patient appears, the more will be gained by proper preparation before surgery is undertaken.

STRICTURES OF THE BILE DUCTS

Symptomatic narrowing of the extrahepatic bile passage results from congenital malformations, inflammation secondary to the impaction of a calculus, or to trauma inflicted by the surgeon. The last, in addition to being preventable, is unfortunately the most important etiologic factor in stricture formation, by virtue of its frequency. Regardless of the etiology, the clinical manifestations are those of obstructive jaundice which, if unrelieved, terminates in biliary cirrhosis.

Congenital Biliary Atresia

The infant with congenital biliary atresia usually appears normal at birth, but with the passage of time jaundice of increasing intensity gives notice that some abnormality exists. During the early period of life weight gain and development proceed normally. At the average age of 6 months the effects of biliary cirrhosis become apparent by interference with growth and development. In surgically uncorrectable or untreated cases the average survival time is 14 months, and rarely we have seen infants with atretic ducts live in excess of 5 years.

Acholic stools are not recognized at times because of the contamination with urine in the diaper. The collection of uncontaminated specimens will reveal the pasty, acholic stools and deeply pigmented urine.

Persistent jaundice in infancy is due to a variety of lesions in addition to biliary atresia. Syphilis, bacterial infections with hemolytic organisms, hepatitis, erythroblastosis fetalis, and obstructive jaundice resulting from mucus plugs or inspissated bile may all produce jaundice and should be considered in the differential diagnosis. Of these, atypical hepatitis and obstruction by inspissated material give the greatest difficulty in diagnosis. We have found duodenal aspiration after stimulation with cholagogues to be helpful in excluding atresia. Rh incompatibilities need not result in erythroblastosis, but at times are responsible for increased hemolysis conducive to inspissation and concentration of bile. The Coombs test may be negative after the first week even though an Rh incompatibility exists.

When there is evidence of persistent obstructive jaundice

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surgical exploration is indicated. The finding of complete atresia of the extrahepatic biliary ducts is indicative of a hopeless situation, for liver biopsy will show the major intrahepatic ducts also to be absent. For this reason anastomosis between the incised left lobe of the liver and the jejunum (Longmire) is ineffective in establishing a pathway for the flow of bile in congenital atresia. In the series from the Boston Children's Hospital, Gross (45) found a surgically correctable situation in 18% of cases. The experience at the St. Louis Children's Hospital is less encouraging. From 1946 to 1956 the diagnosis of biliary atresia was made 21 times; verification at operation or autopsy was possible in 18 patients only. The remaining three cases were examples of inspissation of bile which was relieved after exploratory laparotomy. In only 2 of the 18 cases of atresia was a surgically correctable situation encountered. In 15 cases both the extrahepatic and intrahepatic ducts were atretic; in 1 case, only intrahepatic ducts were involved.

Inflammatory Stricture

As noted above, inflammatory strictures are believed to result from the impaction of stones in the choledochus. This is most likely to occur in the distal portion, particularly in the ampullary region, but even here strictures are rare.

Traumatic Stricture

Nowhere else within the abdomen is the margin of surgical error so narrow as it is in the region of the hepatoduodenal ligament. The close proximity of the bile ducts, hepatic artery and portal vein, as well as the numerous variations in the regional anatomy which are encountered, make this area particularly vulnerable to surgical trauma. In the presence of normal uninflamed structures the dissection of this area is comparatively simple. The addition of cholecystitis, pancreatitis, duodenal ulcer, or a neoplasm will add immeasurably to the difficulties of this dissection. Accidents are prone to occur through failure to appreciate anatomic variations, by excessive bleeding, which obscures the operative field, and by the careless or inaccurate placement of large crushing clamps.

The consequences of injuries to the common bile duct,

portal vein and hepatic artery obviously depend on the site and extent of involvement. For example, acute ligation of the portal vein in normal humans will be fatal in 100% of cases. Because the common bile duct occupies a superficial position in the margin of the hepatoduodenal ligament, it is most frequently injured. When significant injury occurs, obstructive jaundice is the eventual predominant symptom.

When the fact of injury is recognized at the time it is inflicted, the surgeon is in an excellent position to rectify the error with full recovery of the patient. The immediate anastomosis of the cut ends of the common bile duct will, when properly carried out, heal without further difficulty. If the injury is unrecognized, the patient is in most cases destined to have repeated operations for reconstruction of the duct. The important considerations in the reconstruction of the damaged duct include mucosa to mucosa approximation of tissues, preferably between the two ends of the common bile duct, and the avoidance of tension. The value of using the distal end of the duct as well as the technic of its location was emphasized by Lahey (46). When the distal end of the duct cannot be found the same principles should be applied to anastomosis between duct and duodenum or jejunum. The use of the Roux-en-Y procedure has been recommended in order to prevent regurgitation of intestinal contents into the biliary tree. Obstruction rather than regurgitation is, in our opinion, the most frequent source of continued or recurrent symptoms after reconstruction of the common duct.

Ogilvie (47) has stressed the importance of avoiding indiscriminate exploration of the common bile duct, as well as the avoidance of traumatic exploration. The danger of chronic sclerosing choledochitis should serve as a source of emphasis to these warnings. This lesion, as implied in the name, is a condition precipitated by trauma in which diffuse sclerosing obstruction of the bile ducts occurs.

NEOPLASMS OF THE BILIARY TRACT

Gallbladder

Benign tumors of epithelial and connective tissue origin occur in the gallbladder, but are of little clinical significance. With improved contrast media for visualization of the gall-

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bladder the diagnosis of "polyps" of the fundus of the gallbladder has been made with increasing frequency. The lesions which have been seen in our laboratory have consisted of either the exaggerated clubbing of the folds seen in cholesterosis, of hyperplasia of the epithelium with glandular metaplasia, or rarely of papillomatous growths. With the exception of the latter, the lesions appear to be entirely innocent. In the absence of stones, their chance discovery does not, in our opinion, constitute an indication for cholecystectomy. The papillomas tend to be bulkier and are neoplastic. Examples of this type of process associated with infiltrative growth are extremely rare. Papillomas which have entirely filled the lumen of the gallbladder have been reported.

Carcinoma of the gallbladder appears to be decreasing in frequency. In 1931 Graham (48), in urging the prophylactic removal of the gallbladder containing stones, noted that carcinoma of the gallbladder accounted for 8 to 10% of all cases of cancer in the female and that in 8.5% of gallbladders containing stones which were removed at the Barnes Hospital, carcinoma was found. At the present time carcinoma of the gallbladder is no longer included in the 10 most common types of cancer in females in the United States, and the incidence in gallbladders containing stones which are removed at the Barnes Hospital is below 3%. The greatest incidence occurs in the seventh decade of life.

Adenocarcinoma is the most frequent histologic variety, papillary and epidermoid lesions occurring in lesser numbers. The latter are never seen in the absence of stones. Metastasis occurs early, both by direct extension to the liver and through lymphatics to the regional lymph nodes. The latter are located in the hepatoduodenal ligament and head of the pancreas. Direct spread into the adjacent biliary ducts also takes place; when this occurs, it may be difficult to determine the exact primary site.

The diagnosis of carcinoma of the gallbladder is seldom made preoperatively, since the clinical picture is indistinguishable from acute or chronic cholecystitis. Jaundice, when present, is usually progressive and associated with chills and fever. Jaundice has been reported in from 48 to 87% of the cases of carcinoma of the gallbladder. It results from progressive extension of the tumor to the lymph nodes in the region of the hepatoduodenal ligament and is a manifestation of

advanced disease. Most patients will have had episodes of biliary colic, the history frequently going back for many years.

Few patients with infiltrating cancer of the gallbladder will be cured. Even in patients in whom the gallbladder is removable cure is seldom possible and early evidence of persistent disease is inexorably manifest.

While other complications of cholelithiasis are better justifications for prophylactic gallbladder removal the danger of carcinoma cannot be ignored. If the estimate of 6,000 deaths in the United States each year made by Glenn (49) is approximately correct, considerable salvage might have been achieved with earlier operation.

Neoplasms of the Extrahepatic Bile Ducts

Tumors may arise anywhere within the extrahepatic bile ducts from the right or left hepatic duct to the ampulla of Vater. The cystic duct is rarely the site of a primary tumor although it may be secondarily involved from lesions of the gallbladder or the common hepatic duct. The most frequent sites of involvement according to Rolleston (50) are at the ampulla of Vater, and at the junction between the cystic and common hepatic ducts. Glenn (49), however, found a predominance of lesions at the ampulla of Vater without any predilection for the confluence of the ducts. Tumors of the bile ducts are seen more frequently in females than males, but the disproportion is slight. Biliary calculi are found in approximately 50% of the cases.

The histology of the tumors arising in the biliary ducts is similar to that seen in primary tumors of the gallbladder. When tumors are advanced and have invaded contiguous structures, it is difficult to determine in which structure the tumor arose. Lymphatic metastases to portal and peripancreatic lymph nodes occur, but in general, at a later stage in relation to the time of surgical intervention, than is the case in carcinoma of the gallbladder or pancreas. For this reason, the prognosis is better in carcinoma arising in the bile ducts than in carcinoma of the gallbladder.

The most striking clinical manifestation of tumors of the extrahepatic bile ducts is painless obstructive jaundice. Tumors arising at the ampulla of Vater are likely to be ulcerated; accordingly occult blood in the stool is usually present. In the group in which gallstones are absent, the gallbladder will be dilated and may be palpable. Since one

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half the cases have gallstones, it is apparent that failure to palpate the gallbladder is of no differential diagnostic importance.

The exact site of origin is of greatest importance in determining whether the surgeon will be able to attempt a curative or a palliative procedure; or, perhaps, that nothing can be accomplished. Lesions arising at the ampulla are, in general, better differentiated, produce jaundice at an earlier date and offer the best anatomic position for radical removal. As one ascends toward the liver, the prognosis becomes increasingly poor. Tumors in the common hepatic duct are likely to result in contraction so that no dilated duct proximal to the point of obstruction will be available for sidetracking anastomosis. At the time of operation the first measure is the confirmation of the clinical diagnosis. This can be done with varying degrees of ease or difficulty, depending on the coexistence of stones, and the point of origin of the tumor. It may be necessary to open the duodenum in order to confirm the diagnosis; this should be done unhesitatingly if the surgeon is doubtful of the diagnosis. If biopsy and frozen section are carried out, the surgeons must take precautions to avoid contamination of the wound. In the past year we have seen two examples of recurrence of ampullary cancer at a drain site; these were felt to be the result of implantation. The type of operation employed also depends on the point of origin. However, if cure is to be achieved, the radical block removal devised by Whipple should be employed. Local excision of ampullary cancer should be carried out in otherwise operable cases.

The prognosis is poor with the exception of cancer arising in the terminal portion of the common duct or at the ampulla; here 33% of cases should be salvaged. This figure can be increased to 50% by a reduction in operative mortality and a reduction in the incidence of implantation recurrence. Tumors arising at the confluence of the cystic and common hepatic ducts are seldom cured, and tumors of the hepatic ducts are almost hopeless.

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